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(54) **SUPPORT VESSELS FOR SINGLE USE BIOREACTORS AND MIXERS**

STÜTZBEHÄLTER FÜR EINWEGBIOREAKTOREN UND -MISCHER

RÉCIPIENTS DE SUPPORT POUR BIORÉACTEURS ET MÉLANGEURS À USAGE UNIQUE

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Description

Technical field of the invention

[0001] The present invention relates to single use bioreactors and mixers for use in bioprocess applications and in particular to support vessels for such single use bioreactors and mixers. The invention also relates to hollow profile segments and sections that can be assembled to form side walls of support vessels.

Background of the invention

[0002] In the bioprocess field, bioreactors and mixers are typically designed as jacketed allowing for heat transfer to achieve temperature control for process liquids such as cell cultures, cell culture media or buffers by either cooling or heating a heat exchange (HX) fluid circulating through the jacket. This design is applied also to single-use applications where the internal of the vessel is fitted with a single use closed plastic bag holding the liquid. One such system is disclosed in US2015029815A1 (GE Healthcare Biosciences AB), which describes a mixing system comprising a vessel for housing a disposable fluid mixing bag where the vessel comprises a base supporting the fluid mixing bag and a sidewall with double walls within which a heated or cooled liquid is arranged to flow.

[0003] The cost of the re-usable jacketed tank used in single-use applications, however, is equally expensive as the equivalent equipment in traditional (non-single use) processes as the design principles and manufacturing technologies for building the jacketed applied today are identical. Stainless steel constructions are laminated by extensive welding operations.

[0004] US4197689 (DeMuth Steel Products company) discloses a storage vessel suitable for storing agricultural products, chemicals and other bulk mineral products, where said vessel is constructed by assembling a plurality of sheet metal wall segments to form circular sub-assemblies which are then flange interconnected to provide a cylindrical vessel. However, said cylindrical vessel would not be suitable for use in the field of bioreactors where temperature control feature is required.

[0005] Accordingly, there is a need for a more cost-efficient design of jacketed support vessels for single use flexible bags, in order to fully exploit the simplicity and cost reductions enabled by single-use technology.

Summary of the invention

[0006] Inexpensive hollow (e.g. extruded) extruded profiles can be used to produce elongated hollow structures that serve as conduits for the heat exchange fluid. By arranging multiple hollow profiles adjacent to each other, a wall structure can be formed that resembles a conventional jacketed wall of a vessel.

[0007] The scope of the invention is defined in the ap-

ended set of claims. The alternative design can take advantage of the fact that the fluid is no longer in direct contact with the vessel wall when employing single-use bags. Materials and surface structures can thereby be different compared to traditional processing equipment.

[0008] One aspect of the invention is to provide a hollow profile wall segment allowing the cost-effective construction of a jacketed bioreactor or mixer support vessel. This is achieved with a wall segment comprising a base profile with two parallel wide sides, two narrow sides and at least one heat exchange channel which extends in a longitudinal direction of the base profile through an interior space in the profile. The wall segment is adapted to be joined with similar wall segments to form a side wall of a bioreactor or mixer support vessel and each narrow side comprises at least one coupling member capable of securing the wall segment side by side with similar wall segments.

[0009] One advantage is that the manufacturing cost of the profiles is low. Further advantages are that they can easily be assembled to form jacketed vessel walls and that it is possible to provide a wide range of different flow path patterns.

[0010] A second aspect of the invention is a side wall of a bioreactor or mixer support vessel, which comprises a plurality of hollow profile wall segments, each comprising a base profile with two parallel wide sides, two narrow sides and at least one heat exchange channel extending in a longitudinal direction of the base profile through an interior space in the base profile, where the wall segments are joined side by side.

[0011] A third aspect of the invention is to provide a bioreactor or mixer support vessel comprising a side wall as discussed above, a bottom wall and top and bottom distribution manifolds, fluidically connecting a plurality of the heat exchange channels with an inlet and an outlet.

[0012] A fourth aspect of the invention is to provide a bioreactor or mixer comprising a flexible bag mounted in a support vessel as discussed above.

[0013] A fifth aspect of the invention is to provide hollow profile wall section for a cylindrical bioreactor or mixer support vessel, which comprises a base tubular section with an inner surface, an outer surface and a plurality of heat exchange channels extending in an axial direction through the base tubular section, wherein the wall section is arranged to be stacked with similar wall sections.

[0014] A sixth aspect of the invention is to provide a cylindrical side wall of a bioreactor or mixer support vessel, comprising a plurality of stacked hollow profile wall sections as discussed above, wherein the heat exchange channels of the stacked sections are in register with each other.

[0015] A seventh aspect of the invention is to provide a bioreactor or mixer support vessel comprising the cylindrical side wall as discussed above, a bottom wall and top and bottom distribution manifolds, fluidically connecting a plurality of the heat exchange channels with an inlet and an outlet

[0016] Further suitable embodiments of the invention are described in the dependent claims.

Drawings

[0017]

Fig. 1 shows a hollow profile segment (module) of the invention with locking/coupling elements at both sides. Different alternatives for hollow internal conduits/ heat exchange channels for guiding a HX fluid are shown, here cylindrical and rectangular.

Fig. 2 shows a segment of the invention with a triangular baffle on the side facing inwards.

Fig. 3 shows hollow profile segments (modules) forming a rigid cylindrical vessel side wall comprising heat exchange (HX) functionality.

Fig. 4 shows the side wall of Fig. 3 with additional internal and external covers.

Fig. 5 shows a) an alternative hollow profile segment and b) a rigid cylindrical vessel side wall made up of these segments.

Fig. 6 shows cylindrical support vessels with axially aligned hollow profile segments that are connected to a top and bottom fluid manifold and to a bottom wall. a) parallel connection of heat exchange channels, b) serial connection of heat exchange channels, c) parallel connection with an intermediate manifold.

Fig. 7 shows extruded, ring shaped, elements stacked on top of each other to build a side wall for a cylindrical vessel. Rectangular or other geometries could be made accordingly. The fluid flow inside the elements can be managed both axially and laterally depending on the module configuration and the sealing and intermediate plates that could be stacked in between the extruded modules.

Fig. 8 shows a cylindrical vessel with the side wall of Fig 7 and top and bottom manifolds and a bottom wall.

Fig. 9 shows a bioreactor/mixer of the invention, with a flexible bag mounted in a support vessel.

Fig. 10 shows a hollow profile segment (module) of the invention with an additional insulation channel.

Fig. 11 shows a side wall of the invention with additional insulation channels in the hollow profile segments (modules).

Fig. 12 shows different varieties (cross sections) of locking/coupling elements for segments of the invention. a) Protruding male element and recessed female element, b) Protruding male and female elements, c) Recessed female elements on segments and male elements on separate coupling profile, d) Genderless elements.

Definitions

[0018] To more clearly and concisely describe and point out the subject matter of the claimed invention, the following definitions are provided for specific terms that are used in the following description and the claims appended hereto.

[0019] The singular forms "a" "an" and "the" include plural referents unless the context clearly dictates otherwise. Approximating language, as used herein throughout the specification and claims, may be applied to modify any quantitative representation that could permissibly vary without resulting in a change in the basic function to which it is related. Accordingly, a value modified by a term such as "about" is not to be limited to the precise value specified. Unless otherwise indicated, all numbers expressing quantities of ingredients, properties such as molecular weight, reaction conditions, so forth used in the specification and claims are to be understood as being modified in all instances by the term "about." Accordingly, unless indicated to the contrary, the numerical parameters set forth in the following specification and attached claims are approximations that may vary depending upon the desired properties sought to be obtained by the embodiments of the present invention. At the very least each numerical parameter should at least be construed in light of the number of reported significant digits and by applying ordinary rounding techniques.

[0020] As used herein to describe the present invention, directional terms such as "up", "down", "top", "bottom", "vertical", "horizontal", as well as any other directional terms, refer to those directions of a bioreactor or mixer as used in the normal operational position.

Detailed description of embodiments

[0021] In one aspect, illustrated by Figs. 1-4, the present invention discloses an elongated hollow profile wall segment **1** for a bioreactor or mixer support vessel **2;2a;2b**. The wall segment comprises a base profile **3** with two parallel wide sides **4,5**; two narrow sides **6,7** and at least one heat exchange channel **8** that extends in a longitudinal direction of the base profile through an interior space **9** in the base profile. The length ratio **W/N** of the wide sides to the narrow sides may e.g. be at least about 5, such as at least about 10, and/or the ratio of the segment length **L** to the wide side length **W** may e.g. be at least about 5, such as at least about 10. The base profile may have a substantially constant cross section

geometry along a longitudinal axis **13**, e.g. over at least 80% or at least 90% of the length of the profile or over the entire length of the profile. The wall segment is further adapted to be joined with similar wall segments to form a side wall **12** of a bioreactor or mixer support vessel **2;2a;2b** and each narrow side comprises at least one coupling member **10,11** capable of securing the wall segment side by side with similar wall segments. The segments can comprise along their sides a fixation functionality or coupling member such as recesses, tracks and protrusions. These can be employed to lock the elements against each other, for example by longitudinally sliding the elements into each other or by bending the elements from an attachment to a locking angle. A first narrow side **6** may e.g. comprise a male coupling member **10** and a second narrow side **7** may comprise a female coupling member **11;11a**. The coupling members may e.g. comprise a recess, a track and/or a protrusion. If both coupling members are protruding from the narrow side (as in Figs 1 and 12 b), the joints may have some angular flexibility, which facilitates the joining. In this case it may be desirable to apply seal strips (not shown) over the joint to provide a smooth surface. If one coupling member is protruding and the other recessed in the narrow side (as in Figs. 3 and 12 a), a less flexible joint will be formed and seal strips may not be needed, particularly if the two narrow sides are in abutment with each other. This will also be the case for the embodiments shown in Fig. 12 c), where both segments have recessed female coupling elements **11a** joined together by a separate coupling profile **151** with two male coupling elements **10a** arranged to engage elements **11a** by longitudinally sliding the male coupling elements **10a** into the female coupling elements **11a**. Alternatively, the two narrow sides may each comprise a genderless or hermaphroditic coupling member **150**. The wall segment may be generally shaped as a sector of a circular tubular cylinder (i.e. with a cross section corresponding to a circular arc, with the segment having a concave side **4** and a convex side **5**), which allows for assembly of a circular cylindrical side wall **12;112** with the concave sides **4** forming the inside **18** of the wall and the convex sides **5** forming the outside **19** of the wall. Alternatively, the wall segment may have a generally rectangular shape, with straight sides. This allows for assembly of vessels of polygonal prism shape, such as a right polygonal prism. With a large number of rectangular wall elements, e.g. eight or higher, such a polygonal prism shape may approximate a circular cylindrical shape. In this case, vessel walls of different diameters may be assembled using a single type of wall segment.

[0022] In some embodiments, the hollow profile wall segment is an extruded profile, such as an extruded metal profile or an extruded plastic profile. Aluminium and aluminium alloys are commonly used in extruded profiles and the hollow profile wall segment can suitably be an extruded aluminium or aluminium alloy profile. Alternatively, the hollow profile wall segment may be manufac-

tured from sheet metal, such as stainless steel sheet, e.g. by roll forming and (automated) welding. Metals, such as aluminium or aluminium alloys, have generally high thermal conductivities which is beneficial for the heat transfer efficiency.

[0023] In certain embodiments, the at least one heat exchange channel **8** contains one or more internal baffle elements (not shown). These promote turbulence and thereby achieve good heat transfer from the HX flow path. The baffle elements can e.g. be tortuous inserts acting as static mixer elements, e.g. inserts having a helical structure. Examples of such tortuous inserts are shown in e.g. US3286992 and US3635444. The baffle elements can however also be bulk fillers (particles), elongated structures, Raschig rings etc.

[0024] In some embodiments, illustrated by Fig. 2, one of the wide sides **4** comprises a baffle **17** protruding from the wide side **4** (the concave side if the segment is arc-formed). The baffle may e.g. have a triangular cross section. The baffle can also comprise a longitudinal baffle heat exchange channel **14**, or a heat exchange channel **8** may also extend through the baffle as well as through the main body of the segment. This provides good heat exchange also via the baffle.

[0025] In certain embodiments, illustrated by Figs. 10 and 11, the hollow wall profile segment **1** comprises one or more additional insulation channels **308**. The insulation channel(s) can suitably be located adjacent to one **5** of the wide sides, such as the convex side **5** if the segment has a circular arc cross section. The insulation channel(s) can then be located adjacent the outside **19** of a side wall composed of a plurality of profile segments, while the heat exchange channel(s) **8** for heat exchange fluid can be located near the inside **18** of the wall. This arrangement provides good temperature control and good external insulation. The insulation channel(s) may be filled with a thermal insulation material, such as e.g. a foam (e.g. polyurethane foam) or a fibrous material (e.g. glass wool or mineral wool). The profile segment may have a single insulation channel as shown in Fig. 10, but it may also have a plurality of insulation channels, suitably distributed along the (outer) wide side **5**. The latter arrangement may provide higher mechanical stability due to the presence of internal walls between the insulation channels.

[0026] In a second aspect, illustrated by Figs.3-6, the invention discloses a side wall **12;112** of a bioreactor or mixer support vessel **2;2a;2b;102**, which comprises a plurality of laterally joined hollow profile wall segments **1;101**. The segments, e.g. each segment, comprises a base profile **3;103** with two parallel wide sides **4,5;104,105**, two narrow sides **6,7;106,107** and at least one heat exchange channel **8;108** that extends in a longitudinal direction of the base profile through an interior space **9;109** in the base profile. As above, the length ratio **W/N** of the wide sides to the narrow sides may e.g. be at least about 5, such as at least about 10, and/or the ratio of the segment length **L** to the wide side length **W**

may e.g. be at least about 5, such as at least about 10. The base profile may also have a substantially constant cross section geometry along a longitudinal axis **13**, e.g. over at least 80% or at least 90% of the length of the profile or over the entire length of the profile. The wall segments are joined side by side to form the side wall, e.g. via the coupling members. The joints can suitably be capable of withstanding the hydrostatic pressure from a liquid-filled flexible bag on the inside of the side wall. The wall segments can be as discussed in the embodiments above but they can also have other types of geometries. For example, they can be tubes **103** with rectangular or arc-shaped cross section, a hollow interior (heat exchange channel) **108** and a tube wall composed of two parallel wide sides **104, 105** and two narrow sides **106, 107**. The tubes **103** may be joined side by side, e.g. by welding or soldering the respective narrow sides to each other. The side wall can be cylindrical, e.g. circular cylindrical (i.e. with an essentially circular cross section), or alternatively it can have a polygonal prism shape (i.e. having a polygonal cross section). It can further comprise an external cover **15**, which may e.g. comprise a thermal insulation layer. Alternatively, or additionally, the side wall can also comprise an internal cover **16**, comprising e.g. a sheet-formed material such as a metal sheet, e.g. of stainless steel, or a plastic sheet. If a metal sheet comprising a different metal than the wall segments is used, a non-metallic protective layer or extra sheet may be provided to prevent the formation of galvanic elements. The internal cover can provide a smooth surface for contacting a flexible bag and it may also provide corrosion protection for the wall segments in case of bag leakage. In addition to, or as an alternative to the internal cover, the side wall may comprise a plurality of internal seal strips covering the coupling members to provide a smooth surface. It is also possible to apply one or more support rings (hoops) on the outside **19** or the external cover **15**, to provide additional support against internal pressures.

[0027] In some embodiments, the side wall comprises a plurality of hollow profile wall segments each having a baffle **17** protruding from a wide side **4** on an inside **18** of the side wall and a plurality of hollow profile wall segments without baffles. The baffled segments can suitably be interspersed with non-baffle segments in such a way that the baffles are evenly distributed along the inside of the side wall. The side wall may e.g. comprise 2, 3, 4, 5 or 6 baffles. As discussed above, the baffles may contribute to the heat exchange via baffle heat exchange channels **14** or heat exchange channels **8** extending through the baffles.

[0028] In a third aspect, illustrated by Figs. 6 a) - c), the invention discloses a bioreactor or mixer support vessel **2; 2a; 2b; 102**, comprising the side wall **12; 112** as discussed in the embodiments above. The inner volume of the vessel may e.g. be at least 25 l, such as 25-2000 l, 50-2000 l or 50-1000 l. An advantageous concept to manage the distribution of HX fluid over the individual segments is to build a barrel like construction (for the

example a cylindrical vessel) and to connect the hollow segments at top and bottom to a circular or annular structure that provides mechanical support and fixation, liquid connections and the fluid distribution features desired.

The support vessel comprises a bottom wall **20** and top **21** and bottom **22** distribution manifolds, which may be annular, where the manifolds fluidically connect a plurality of the heat exchange channels **8** with an inlet **23** and an outlet **24**. The manifolds **21, 22**, also called distribution manifolds, are used in order to guide the HX fluid, providing uniform efficiency over the jacketed area of the vessel. The area covered by individual segments is selected such that the temperature loss along the segment is optimal. The top and bottom distribution manifolds may suitably comprise an inlet **23** or outlet **24** fluidically connected to a plurality of heat exchange channel connector ports **25** in register with the heat exchange channels **8**. This arrangement provides a parallel coupling of the heat exchange channels such that heat exchange fluid can pass from the inlet to the outlet via a parallel set of heat exchange channels. Alternatively, the top and bottom distribution manifolds may comprise an inlet **23** fluidically connected to a first heat exchange channel connector port **27a** in register with a first heat exchange channel **8a** and a plurality of heat exchange channel interconnector conduits **26**, each of which is fluidically connected with two adjacent heat exchange channels **8** via heat exchange channel interconnector ports **27** in register with said two adjacent heat exchange channels. A last heat exchange channel **8b** may then be fluidically connected via a last heat exchange channel connector port **27b** to an outlet **24**. This allows serial coupling of the heat exchange channels, such that the heat exchange fluid passes from the inlet through one heat exchange channel after another before reaching the outlet. In addition to the top and bottom manifolds, the support vessel **2b** may also comprise one or more further manifolds **28**, as illustrated by Fig. 6 c), where a third manifold **28** distributes heat exchange fluid from inlet **23** in both upwards and downwards directions via the heat exchange channels **8** to the outlets **24**. It is also possible to arrange fluidic connection between heat exchange channels by lateral ports (not shown) in the wall segments. In this case, at least two adjacent hollow profile wall segments comprise lateral ports, fluidically connecting the heat exchange channels **8** of the segments with each other. This could for example be achieved by creating an opening perpendicular to the direction of extrusion (by drilling or cutting) and fitting a sealing to this opening. Multiple segments could then be joined through such adjacent openings and sealings, the segments could be clamped against each other like the staves of a barrel.

[0029] In a fourth aspect, illustrated by Fig. 9, the invention discloses a bioreactor or mixer comprising a flexible bag **30** mounted in the support vessel **2** as discussed in the embodiments above. The flexible bag may e.g. be manufactured from a plastic laminate and may e.g. be loaded into the vessel from the top of the vessel. In the

interior volume of the bag **33**, cells can be cultivated or process liquids, e.g. buffers can be mixed. Through one or more ports **34** in the bag, fluids can be added and removed as needed in the process. The bag may also comprise a magnetically driven impeller **31** for agitation, which may be driven by a magnetic drive unit **32** in or adjacent to the support vessel. The flexible bag may be supplied pre-sterilized, e.g. by gamma irradiation and may be used a single-use item, obviating the need for cleaning and cleaning validation of reusable vessels. During operation of the bioreactor or mixer, inlet **23** and outlet **24** are suitably fluidically connected to a supply of HX fluid, such that HX fluid of suitable temperature is circulated through the manifolds **21,22,23;221,222** and the heat exchange channels **8,8a,14;208** to maintain the content of the flexible bag **30** (e.g. a cell culture or a process liquid) at a desired temperature. For cell culture, the desired temperature is often in the 30-40 °C range, but temperatures outside this range, e.g. 0-60 °C, may also be used, particularly for mixers or for cultivation of thermophilic or psychrophilic organisms.

[0030] In a fifth aspect, illustrated by Figs. 7-8, the invention discloses a hollow profile wall section **201** for a cylindrical bioreactor or mixer support vessel **202** side wall, which comprises a base tubular section **203** with an inner surface **204**, an outer surface **205** and a plurality of heat exchange channels **208** extending in an axial direction through the base tubular section, wherein the hollow profile wall section is arranged to be stacked with similar hollow profile wall sections. The tubular sections could be annular, but they could also cover a larger or substantially the complete cylindrical surface to provide also a bottom structure of a vessel, for example. The tubular sections may be manufactured e.g. by extrusion, such as by extrusion of aluminium or an aluminium alloy.

[0031] In a sixth aspect, illustrated by Figs. 7-8, the invention discloses a cylindrical side wall **202** of a bioreactor or mixer support vessel, comprising a plurality of stacked hollow profile wall sections as discussed in the embodiments above, wherein the heat exchange channels of the stacked sections are in register with each other.

[0032] In a seventh aspect, illustrated by Fig. 8, the invention discloses a bioreactor or mixer support vessel comprising a cylindrical side wall **202** as discussed in the embodiments above, a bottom wall **220** and top **221** and bottom **222** distribution manifolds, fluidically connecting a plurality of the heat exchange channels with an inlet **223** and an outlet **224**. Although Fig. 8 shows a parallel flow arrangement, it is equally possible to obtain serial flow by an arrangement analogous to Fig. 6 b). Further, a flexible bag may be mounted in the support vessel as illustrated in Fig. 9, to be used as a bioreactor or mixer as discussed above for the vessels having side walls made up of segments joined side by side.

[0033] In an eighth aspect, the invention discloses a method of cultivating cells in the bioreactors disclosed above. The method comprises providing a bioreactor with

a flexible bag as discussed above. The flexible bag can suitably be supplied pre-sterilized. The method further comprises adding cells and culture medium to the flexible bag, suitably under aseptic conditions and cultivating said cells in the flexible bag. Cultivation of said cells is done suitably under agitation with addition and removal of gases (e.g. air and carbon dioxide) and under thermostatic conditions.

Claims

1. A hollow profile wall segment (1) for a bioreactor or mixer support vessel (2;2a;2b), comprising an extruded aluminium or aluminium alloy base profile (3) with two parallel wide sides (4,5), two narrow sides (6,7) and at least one heat exchange channel (8) extending in a longitudinal direction of said base profile through an interior space (9) in said base profile, wherein said hollow profile wall segment is adapted to be joined with similar hollow profile wall segments to form a side wall (12) of a bioreactor or mixer support vessel (2) and wherein each narrow side comprises at least one coupling member (10,11;11a;150) capable of securing said hollow profile wall segment side by side with similar hollow profile wall segments.
2. The hollow profile wall segment of claim 1, wherein said at least one heat exchange channel contains one or more internal baffle elements.
3. The hollow profile wall segment of any preceding claim, wherein a first narrow side (6) comprises a male coupling member (10) and a second narrow side (7) comprises a female coupling member (11), and/or wherein said coupling member comprises a recess, a track or a protrusion.
4. The hollow profile wall segment of any preceding claim, wherein one of said wide sides (4) comprises a baffle (17) protruding from said wide side (4) wherein optionally said baffle has a triangular cross section.
5. The hollow profile wall segment of any preceding claim, generally shaped as a sector of a circular tubular cylinder, or which is generally rectangular.
6. The hollow profile wall segment of any preceding claim, further comprising one or more insulation channels (308), optionally comprising a thermal insulation material in said one or more insulation channels.
7. A side wall (12;112) of a bioreactor or mixer support vessel (2;2a;2b;102), comprising a plurality of hollow profile wall segments (1;101) as defined in any pre-

ceding claim, wherein said plurality of hollow profile wall segments (1;101) are joined side by side.

8. The side wall of claim 7, further comprising:

- a) an external cover (15);
- b) an internal cover (16); and/or
- c) a plurality of internal seal strips covering said coupling members.

9. The side wall of claim 7 or 8, comprising a plurality of hollow profile wall segments each having a baffle protruding from a wide side (4) on an inside (17) of said cylindrical wall and a plurality of hollow profile wall segments without baffles.

10. A bioreactor or mixer support vessel (2;2a;2b) comprising the side wall of any one of claims 7-9, a bottom wall (20) and top (21) and bottom (22) distribution manifolds, fluidically connecting a plurality of said heat exchange channels with an inlet (23) and at least one outlet (24), wherein optionally said top and bottom distribution manifolds are annular.

11. The support vessel of claim 10, wherein:

- a) said top and bottom distribution manifolds comprise an inlet or outlet fluidically connected to a first heat exchange channel connector port in register with a first heat exchange channel (8a) and a plurality of heat exchange channel interconnector conduits (26), each fluidically connected with two adjacent heat exchange channels (8) via heat exchange channel interconnector ports (27);
- b) the support vessel further comprises a third distribution manifold (28), fluidically connecting a plurality of said heat exchange channels (8) with an inlet (23) or an outlet (24); and/or
- c) at least two adjacent hollow profile wall segments comprise lateral ports, fluidically connecting the heat exchange channels (8) of said segments with each other.

12. A hollow profile wall section (201) for a cylindrical bioreactor or mixer support vessel, comprising a base tubular section (203) with an inner surface (204), an outer surface (205) and a plurality of heat exchange channels (208) extending in an axial direction through said base tubular section, wherein said hollow profile wall section is arranged to be stacked with similar hollow profile wall sections, wherein said base tubular section is an extruded aluminium or aluminium alloy section.

13. A cylindrical side wall (202) of a bioreactor or mixer support vessel, comprising a plurality of stacked hollow profile wall sections according to claim 12,

wherein the heat exchange channels of the stacked sections are in register with each other.

14. A bioreactor or mixer support vessel comprising the cylindrical side wall (202) of claim 13, a bottom wall (220) and top (221) and bottom (222) distribution manifolds, fluidically connecting a plurality of said heat exchange channels (208) with an inlet (223) and an outlet (224).

15. A bioreactor or mixer comprising the support vessel of any one of claims 10, 11 and 14 and a flexible bag (30) mounted in said support vessel.

16. A method of cell cultivation, comprising the steps of:

- a) providing the bioreactor of claim 15;
- b) adding cells and culture medium to said flexible bag; and
- c) cultivating cells in said flexible bag.

Patentansprüche

- 1.** Hohlprofilwandsegment (1) für einen Stützbehälter (2; 2a; 2b) eines Bioreaktors oder Mischers, ein Grundprofil (3) aus extrudiertem Aluminium oder Aluminiumlegierung mit zwei parallelen Breitseiten (4, 5), zwei Schmalseiten (6, 7) und mindestens einem Wärmetauschkanal (8) umfassend, der sich in einer Längsrichtung des Grundprofils durch einen Innenraum (9) in dem Grundprofil erstreckt, wobei das Hohlprofilwandsegment angepasst ist, um mit ähnlichen Hohlprofilwandsegmenten verbunden zu werden, um eine Seitenwand (12) eines Stützbehälters (2) eines Bioreaktors oder Mischers zu bilden, und wobei jede Schmalseite mindestens ein Kopp­ lungsglied (10, 11; 11a; 150) umfasst, das imstande ist, das Hohlprofilwandsegment Seite an Seite mit ähnlichen Hohlprofilwandsegmenten zu befestigen.
- 2.** Hohlprofilwandsegment nach Anspruch 1, wobei der mindestens eine Wärmetauschkanal ein oder mehrere innere Umlenkelemente enthält.
- 3.** Hohlprofilwandsegment nach einem vorstehenden Anspruch, wobei eine erste Schmalseite (6) ein Steckkopplungsglied (10) umfasst, und eine zweite Schmalseite (7) ein Buchsenkopplungsglied (11) umfasst, und/ oder wobei das Kopplungsglied eine Aussparung, eine Spur oder eine Erhebung umfasst.
- 4.** Hohlprofilwandsegment nach einem vorstehenden Anspruch, wobei eine der Breitseiten (4) eine Umlenkung (17) umfasst, die aus der Breitseite (4) hervorsteht, wobei die Umlenkung optional einen dreieckigen Querschnitt aufweist.

5. Hohlprofilwandsegment nach einem vorstehenden Anspruch, das im Allgemeinen als Sektor eines kreisförmigen Rohrzylinders geformt ist, oder das im Allgemeinen rechteckig ist.
6. Hohlprofilwandsegment nach einem vorstehenden Anspruch, weiter einen oder mehrere Dämmkanäle (308) umfassend, die optional ein Wärmedämmmaterial in dem einen oder mehreren Dämmkanälen umfassen.
7. Seitenwand (12; 112) eines Stützbehälters (2; 2a; 2b; 102) eines Bioreaktors oder Mischers, eine Vielzahl von Hohlprofilwandsegmenten (1; 101) nach einem vorstehenden Anspruch umfassend, wobei die Vielzahl von Hohlprofilwandsegmenten (1; 101) Seite an Seite verbunden sind.
8. Seitenwand nach Anspruch 7, weiter umfassend:
- a) eine äußere Abdeckung (15);
 - b) eine innere Abdeckung (16); und/ oder
 - c) eine Vielzahl von inneren Dichtstreifen, die die Kopplungsglieder abdecken.
9. Seitenwand nach Anspruch 7 oder 8, eine Vielzahl von Hohlprofilwandsegmenten umfassend, von denen jedes eine Umlenkung aufweist, die aus einer Breitseite (4) an einer Innenseite (17) der zylindrischen Wand hervorsteht, und eine Vielzahl von Hohlprofilwandsegmenten ohne Umlenkungen.
10. Stützbehälter (2; 2a; 2b) eines Bioreaktors oder Mischers, eine Seitenwand nach einem der Ansprüche 7-9, eine Bodenwand (20) und obere (21) und untere (22) Verteilungssammelleitungen umfassend, die fluidisch eine Vielzahl der Wärmetauschkkanäle mit einem Einlass (23) und mindestens einem Auslass (24) verbindet, wobei optional die oberen und unteren Verteilungssammelleitungen ringförmig sind.
11. Stützbehälter nach Anspruch 10, wobei:
- a) die oberen und unteren Verteilungssammelleitungen einen Einlass oder Auslass umfassen, die fluidisch mit einem ersten Wärmetauschkkanal-Anschlussport in Ausrichtung mit mindestens einem Wärmetauschkkanal (8a) und einer Vielzahl von Wärmetauschkkanal-Verbindungsleitungen (26) verbunden sind, von denen jede fluidisch über die Wärmetauschkkanal-Anschlussports (27) mit zwei angrenzenden Wärmetauschkkanälen (8) verbunden ist;
 - b) der Stützbehälter weiter eine dritte Verteilungssammelleitung (28) umfasst, die fluidisch eine Vielzahl von Wärmetauschkkanälen (8) mit einem Einlass (23) oder einem Auslass (24) verbindet;
- bindet;
und/oder
c) mindestens zwei angrenzende Hohlprofilwandsegmente Seitenports umfassen, die die Wärmetauschkkanäle (8) der Segmente fluidisch miteinander verbinden.
12. Hohlprofilwandsektion (201) für einen zylindrischen Stützbehälter eines Bioreaktors oder Mischers, eine rohrförmige Grundsektion (203) mit einer Innenoberfläche (204), einer Außenoberfläche (205) und einer Vielzahl von Wärmetauschkkanälen (208) umfassend, die sich in einer axialen Richtung durch die rohrförmige Grundsektion erstrecken, wobei die Hohlprofilwandsektion angeordnet ist, um mit ähnlichen Hohlprofilwandsektionen gestapelt zu werden, wobei die rohrförmige Grundsektion eine extrudierte Sektion aus Aluminium oder Aluminiumlegierung ist.
13. Zylindrische Seitenwand (202) eines Stützbehälters eines Bioreaktors oder Mischers, eine Vielzahl von gestapelten Hohlprofilwandsektionen nach Anspruch 12 umfassend, wobei die Wärmetauschkkanäle der gestapelten Sektionen in Ausrichtung miteinander sind.
14. Stützbehälter eines Bioreaktors oder Mischers, eine zylindrische Seitenwand (202) nach Anspruch 13, eine Bodenwand (220), und obere (221) und untere (222) Verteilungssammelleitungen umfassend, die fluidisch eine Vielzahl der Wärmetauschkkanäle (208) mit einem Einlass (223) und mindestens einem Auslass (224) verbinden.
15. Bioreaktor oder Mischer, den Stützbehälter nach einem der Ansprüche 10, 11 und 14, und einen flexiblen Beutel (30), der in dem Stützbehälter angebracht ist, umfassend.
16. Verfahren zur Zellkultivierung, die folgenden Schritte umfassend:
- a) Bereitstellen des Bioreaktors nach Anspruch 15;
 - b) Begeben von Zellen und Kulturmedium in den flexiblen Beutel; und
 - c) Kultivieren von Zellen in dem flexiblen Beutel.
- Revendications**
1. Segment de paroi à profilé creux (1) destiné à un récipient de support de bioréacteur ou de mélangeur (2 ; 2a ; 2b), comprenant un profilé de base en aluminium extrudé ou en alliage d'aluminium (3) doté de deux côtés larges parallèles (4, 5), de deux côtés étroits (6, 7) et d'au moins un canal d'échange thermique (8) s'étendant dans une direction longitudina-

- le dudit profilé de base à travers un espace intérieur (9) dans ledit profilé de base, dans lequel ledit segment de paroi à profilé creux est adapté pour être assemblé à des segments de paroi à profilé creux similaires pour former une paroi latérale (12) d'un récipient de support de bioréacteur ou de mélangeur (2) et dans lequel chaque côté étroit comprend au moins un élément de couplage (10, 11; 11a; 150) pouvant fixer ledit segment de paroi à profilé creux côte à côte à des segments de paroi à profilé creux similaires.
2. Segment de paroi à profilé creux selon la revendication 1, dans lequel ledit au moins un canal d'échange thermique contient un ou plusieurs éléments déflecteurs internes.
 3. Segment de paroi à profilé creux selon l'une quelconque des revendications précédentes, dans lequel un premier côté étroit (6) comprend un élément de couplage mâle (10) et un second côté étroit (7) comprend un élément de couplage femelle (11), et/ou dans lequel ledit élément de couplage comprend un évidement, une piste ou une saillie.
 4. Segment de paroi à profilé creux selon l'une quelconque des revendications précédentes, dans lequel l'un desdits côtés larges (4) comprend un déflecteur (17) faisant saillie à partir dudit côté large (4) dans lequel facultativement ledit déflecteur présente une section transversale de forme triangulaire.
 5. Segment de paroi à profilé creux selon l'une quelconque des revendications précédentes, généralement en forme de secteur d'un cylindre tubulaire de forme circulaire, ou qui est généralement de forme rectangulaire.
 6. Segment de paroi à profilé creux selon l'une quelconque des revendications précédentes, comprenant en outre un ou plusieurs canaux d'isolation (308), comprenant facultativement un matériau d'isolation thermique dans ledit un ou plusieurs canaux d'isolation.
 7. Paroi latérale (12; 112) d'un récipient de support de bioréacteur ou de mélangeur (2 ; 2a ; 2b ; 102), comprenant une pluralité de segments de paroi à profilé creux (1; 101) tels que définis selon l'une quelconque des revendications précédentes, dans laquelle ladite pluralité de segments de paroi à profilé creux (1; 101) sont assemblés côte à côte.
 8. Paroi latérale selon la revendication 7, comprenant en outre :
 - a) un couvercle externe (15) ;
 - b) un couvercle interne (16) ; et/ou
 - c) une pluralité de bandes d'étanchéité internes recouvrant lesdits éléments de couplage.
 9. Paroi latérale selon la revendication 7 ou 8, comprenant une pluralité de segments de paroi à profilé creux présentant chacun un déflecteur faisant saillie à partir d'un côté large (4) sur une partie intérieure (17) de ladite paroi cylindrique et une pluralité de segments de paroi à profilé creux sans déflecteur.
 10. Récipient de support de bioréacteur ou de mélangeur (2 ; 2a ; 2b) comprenant la paroi latérale selon l'une quelconque des revendications 7-9, une paroi inférieure (20) et des collecteurs de distribution supérieur (21) et inférieur (22), reliant de manière fluide une pluralité desdits canaux d'échange thermique à une entrée (23) et au moins une sortie (24), dans lequel facultativement lesdits collecteurs de distribution supérieur et inférieur sont de forme annulaire.
 11. Récipient de support selon la revendication 10, dans lequel :
 - a) lesdits collecteurs de distribution supérieur et inférieur comprennent une entrée et une sortie reliées de manière fluide à un premier port de connecteur de canal d'échange thermique en alignement avec un premier canal d'échange thermique (8a) et une pluralité de conduits d'interconnexion de canaux d'échange thermique (26), chacun étant relié de manière fluide à deux canaux d'échange thermique adjacents (8) par l'intermédiaire de ports d'interconnexion de canaux d'échange thermique (27) ;
 - b) le récipient de support comprend en outre un troisième collecteur de distribution (28), reliant de manière fluide une pluralité desdits canaux d'échange thermique (8) à une entrée (23) ou une sortie (24) ; et/ou
 - c) au moins deux segments de paroi à profilé creux adjacents comprennent des ports latéraux, reliant de manière fluide les canaux d'échange thermique (8) desdits segments les uns aux autres.
 12. Section de paroi à profilé creux (201) destinée à un récipient de support de bioréacteur ou de mélangeur cylindrique, comprenant une section tubulaire de base (203) dotée d'une surface interne (204), d'une surface externe (205) et d'une pluralité de canaux d'échange thermique (208) s'étendant dans une direction axiale à travers ladite section tubulaire de base, dans laquelle ladite section de paroi à profilé creux est agencée pour être empilée avec des sections de paroi à profilé creux similaires, dans laquelle ladite section tubulaire de base est une section en aluminium extrudé ou en alliage d'aluminium.

13. Paroi latérale cylindrique (202) d'un récipient de support de bioréacteur ou de mélangeur, comprenant une pluralité de sections de paroi à profilé creux empilées selon la revendication 12, dans laquelle les canaux d'échange thermique des sections empilées sont alignés les uns aux autres. 5
14. Récipient de support de bioréacteur ou de mélangeur comprenant la paroi latérale cylindrique (202) selon la revendication 13, une paroi inférieure (220) et des collecteurs de distribution supérieur (221) et inférieur (222), reliant de manière fluide une pluralité desdits canaux d'échange thermique (208) à une entrée (223) et une sortie (224). 10 15
15. Bioréacteur ou mélangeur comprenant le récipient de support selon l'une quelconque des revendications 10, 11 et 14 et une poche souple (30) montée dans ledit récipient de support. 20
16. Procédé de culture cellulaire, comprenant les étapes consistant à : 25
- a) fournir le bioréacteur selon la revendication 15 ; 25
 - b) ajouter des cellules et un milieu de culture à ladite poche souple ; et
 - c) mettre en culture des cellules dans ladite poche souple. 30
- 35
- 40
- 45
- 50
- 55

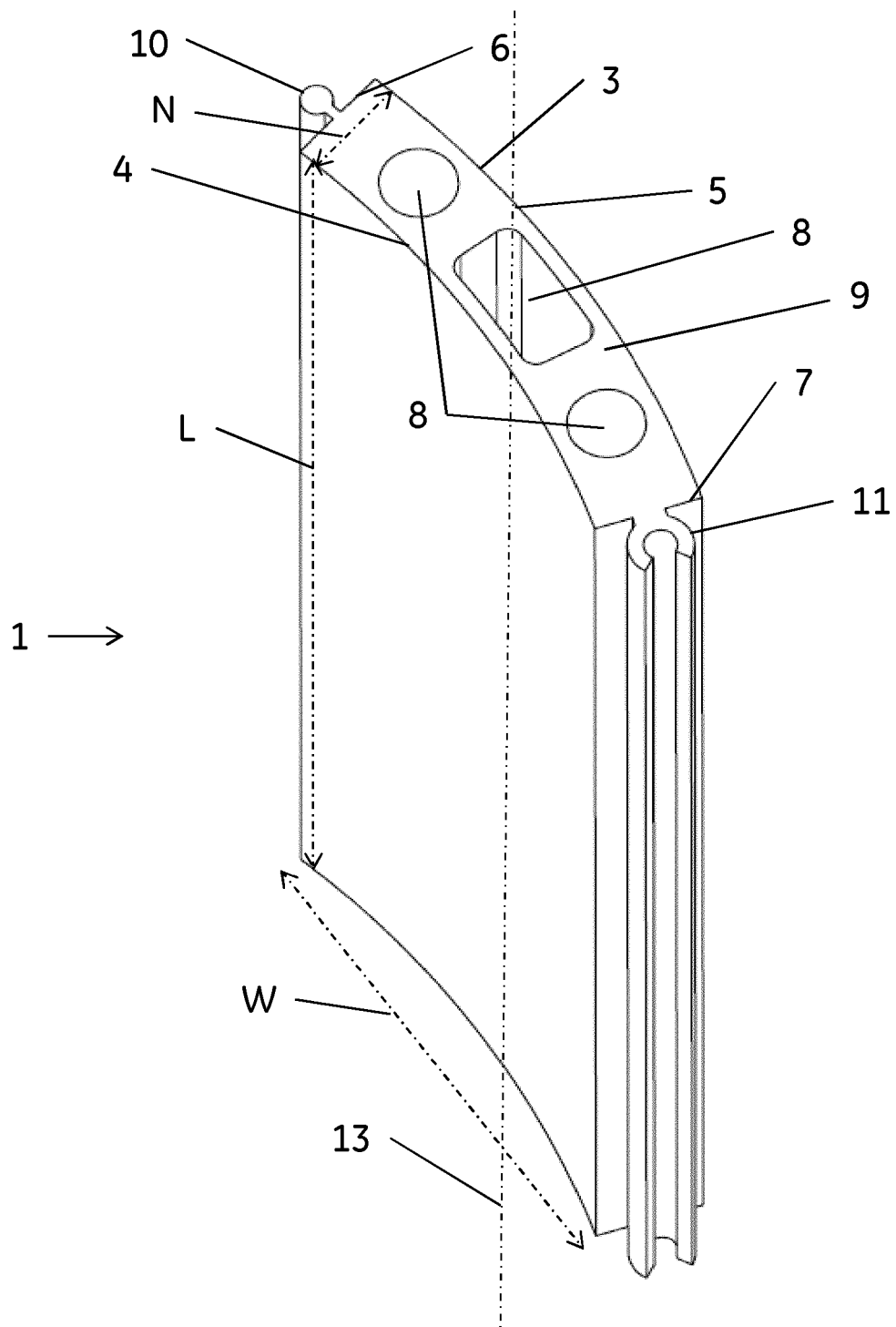


Fig. 1

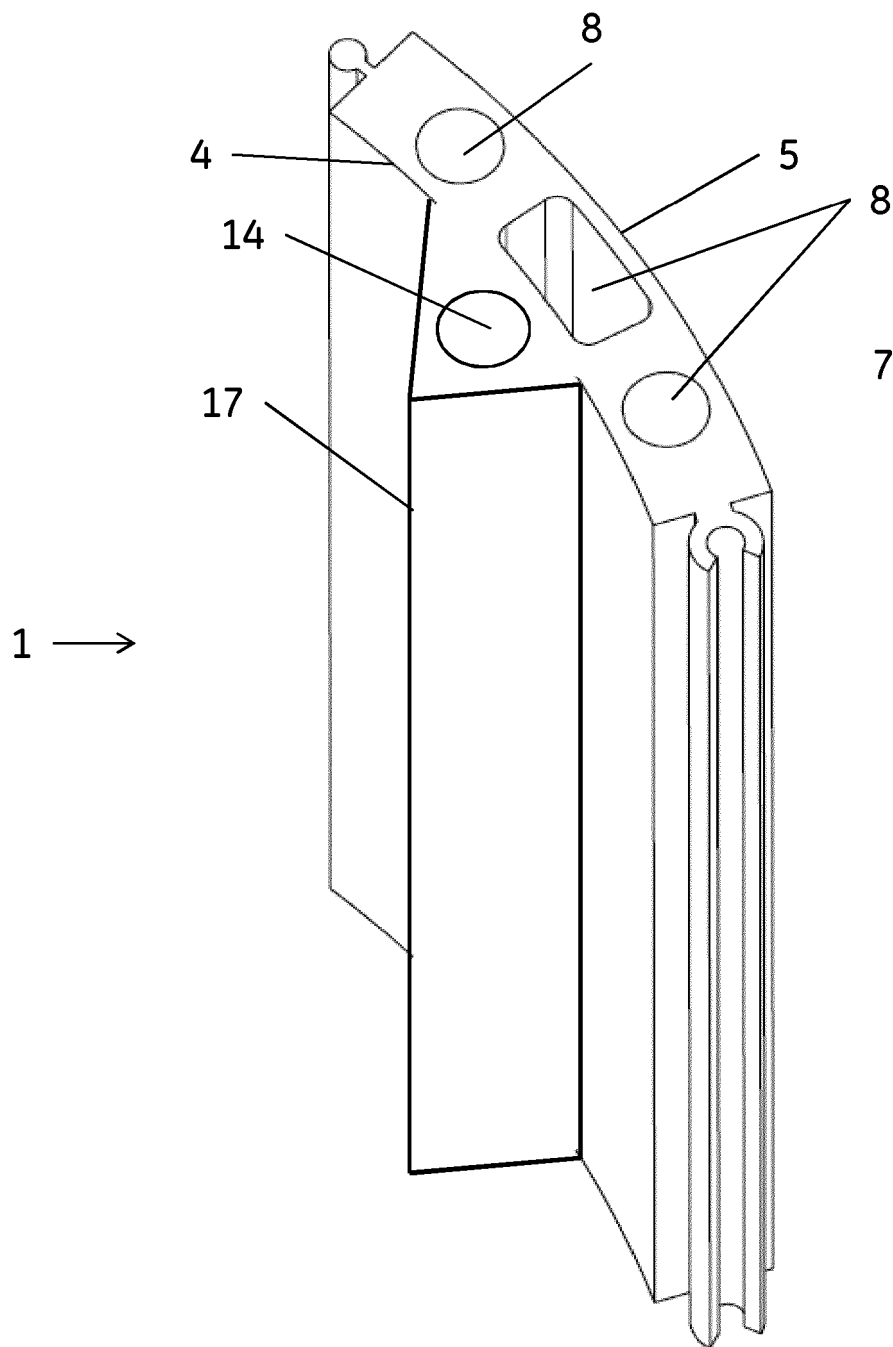


Fig. 2

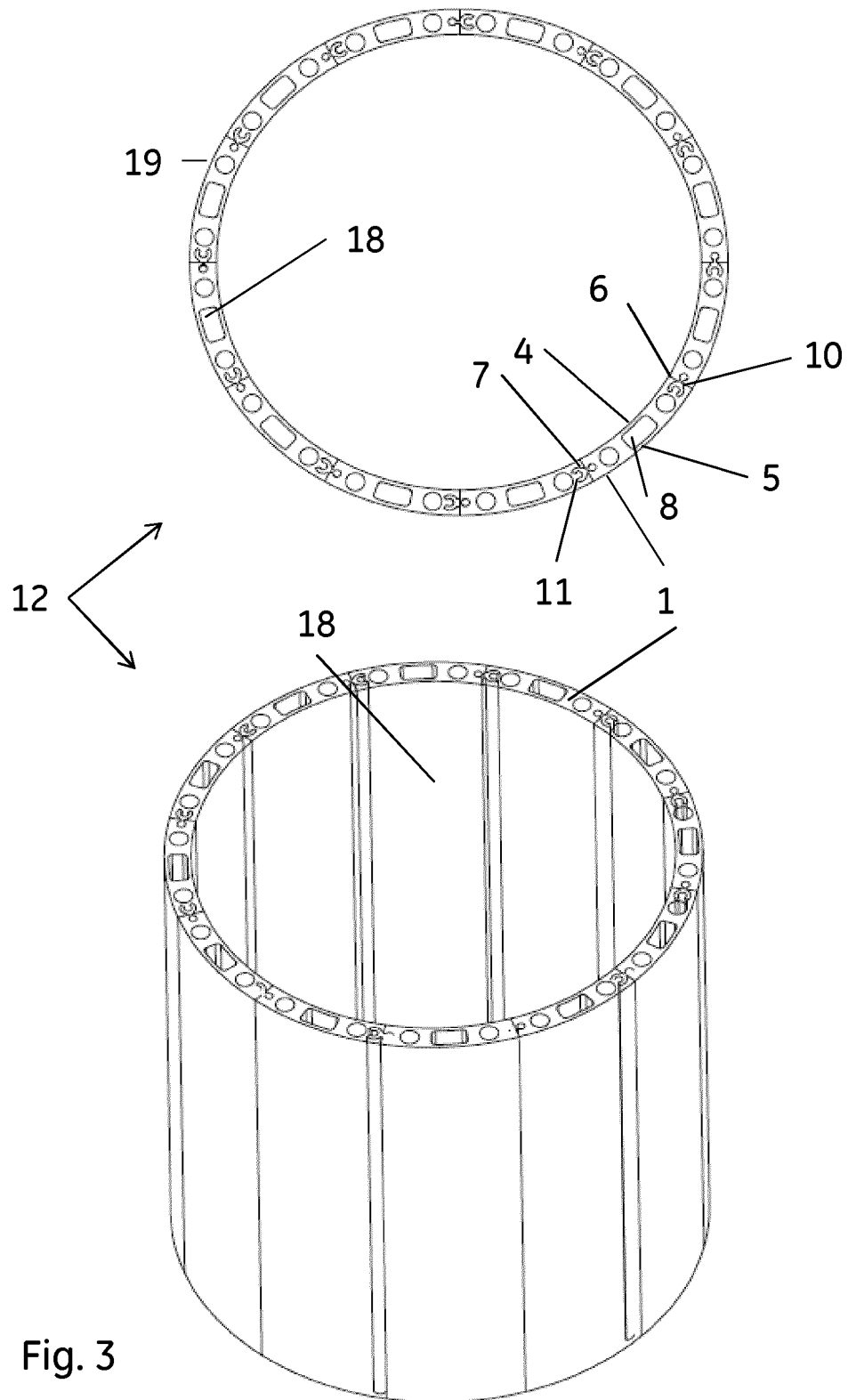
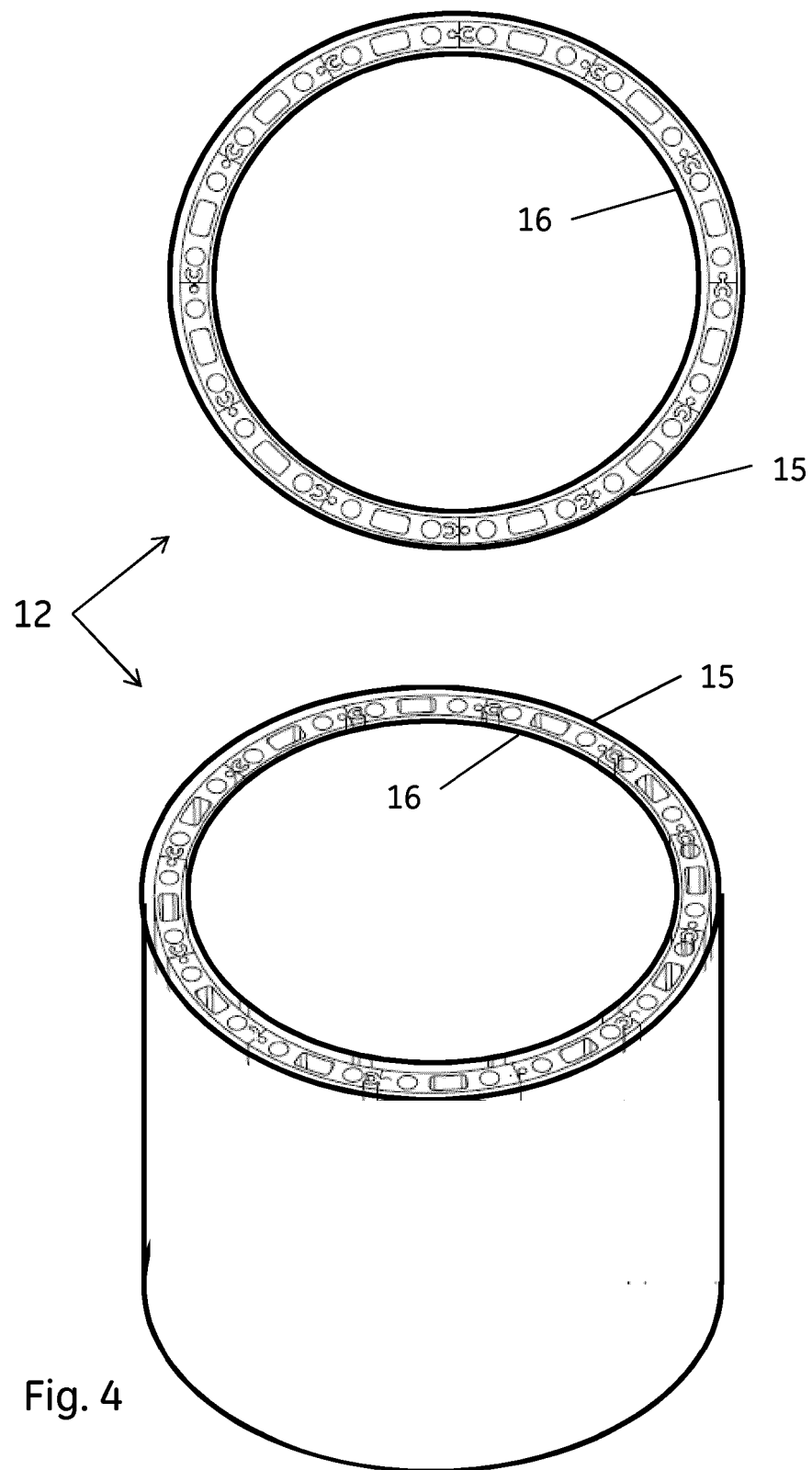


Fig. 3



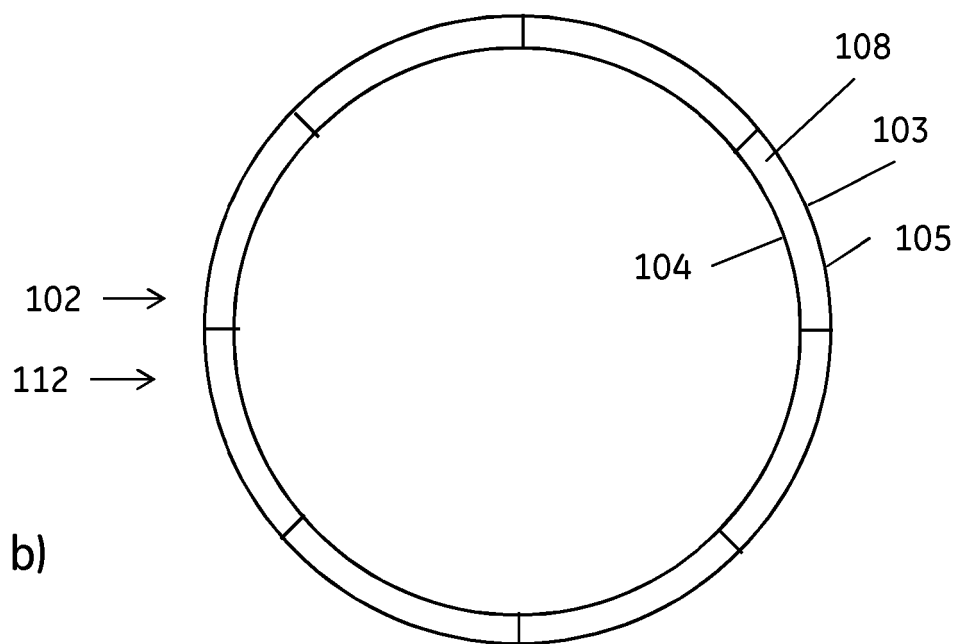
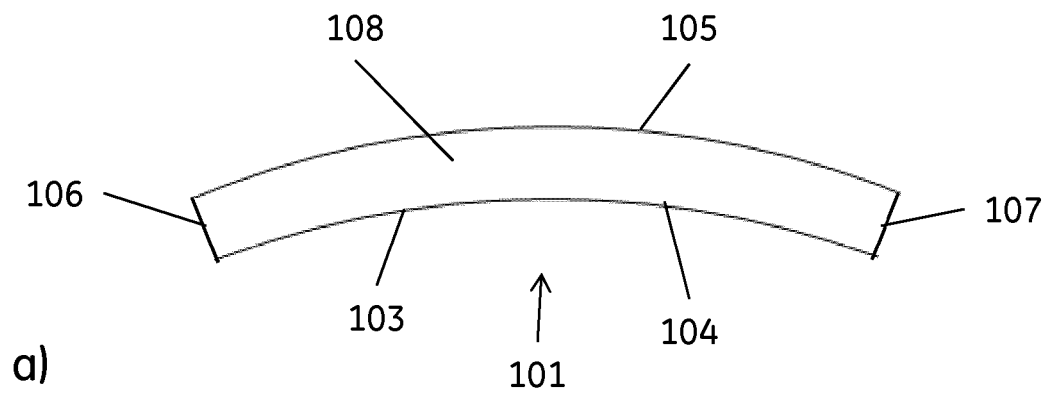


Fig. 5

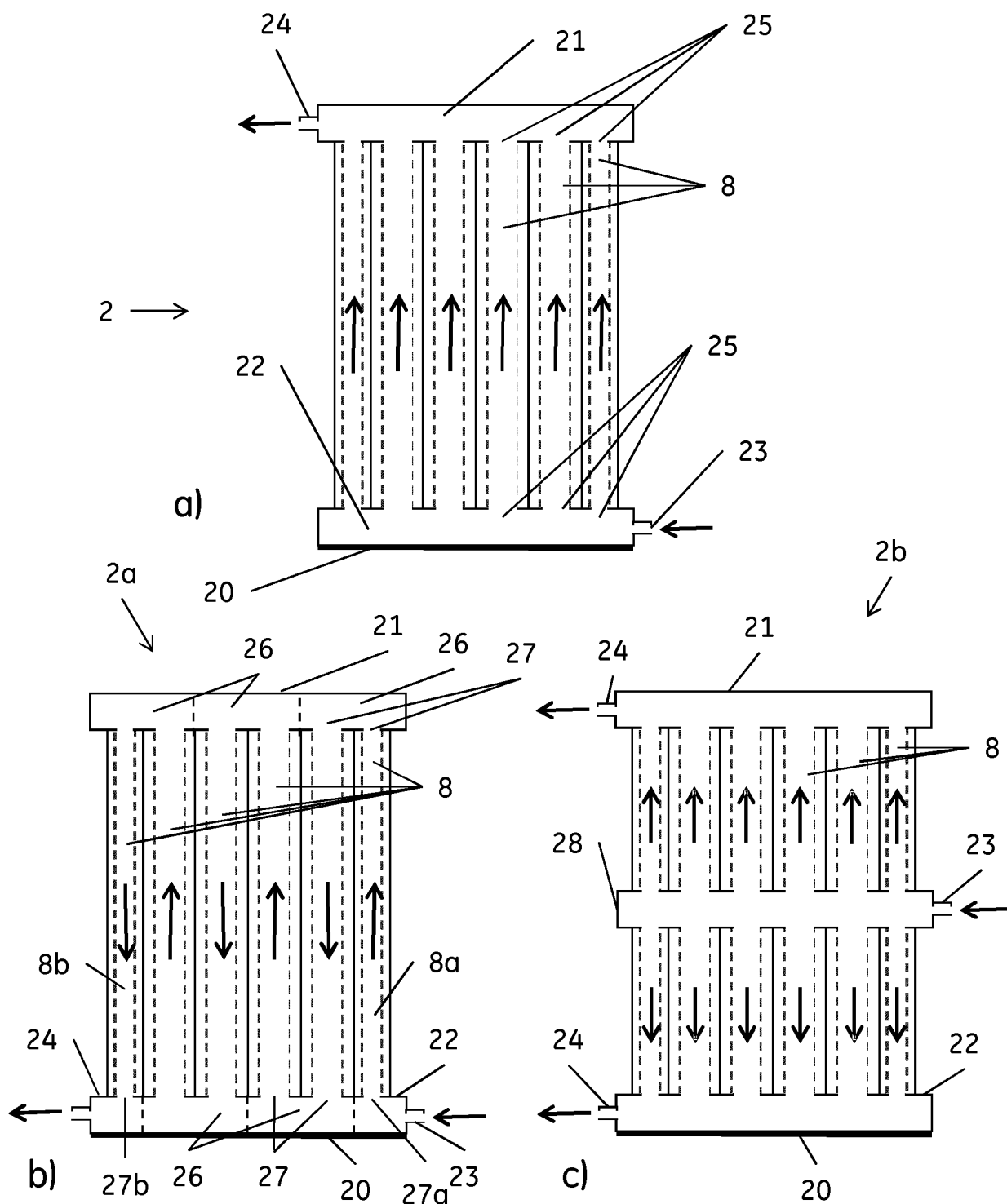


Fig. 6

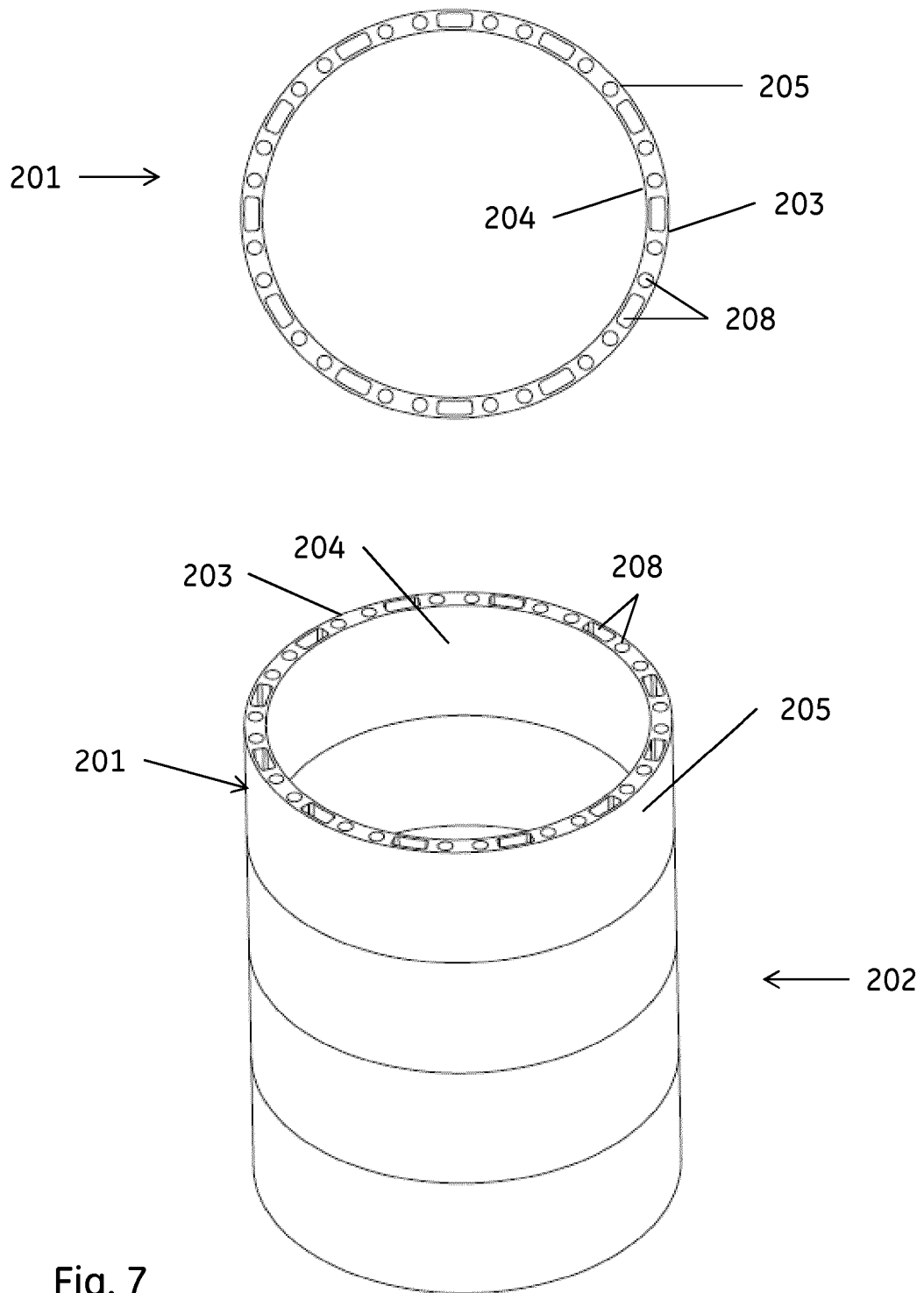


Fig. 7

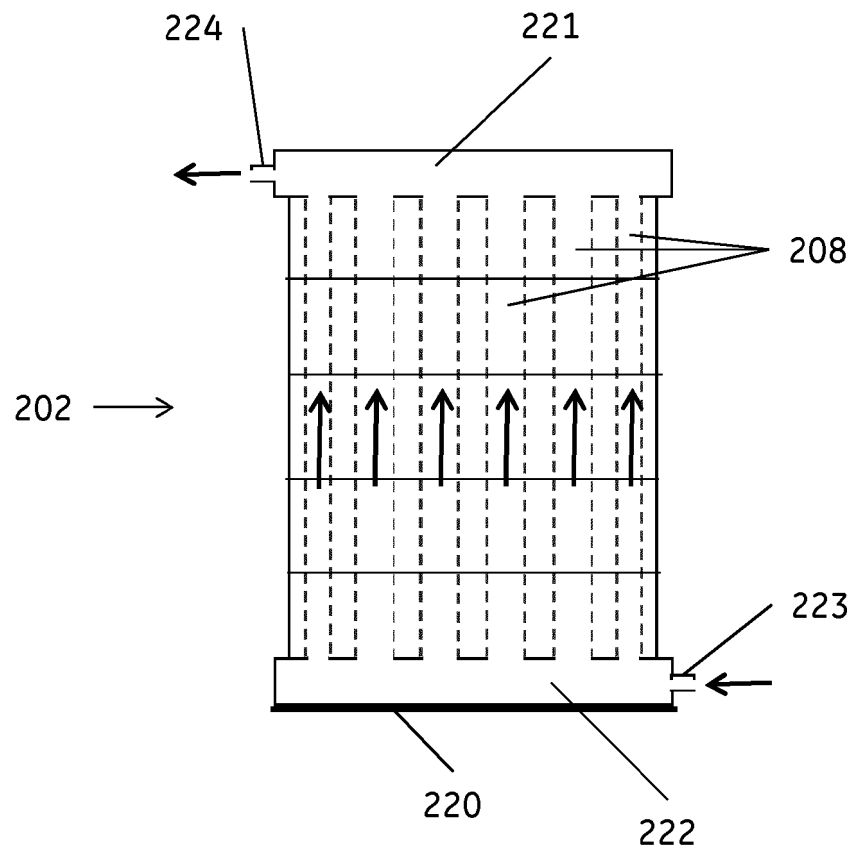


Fig. 8

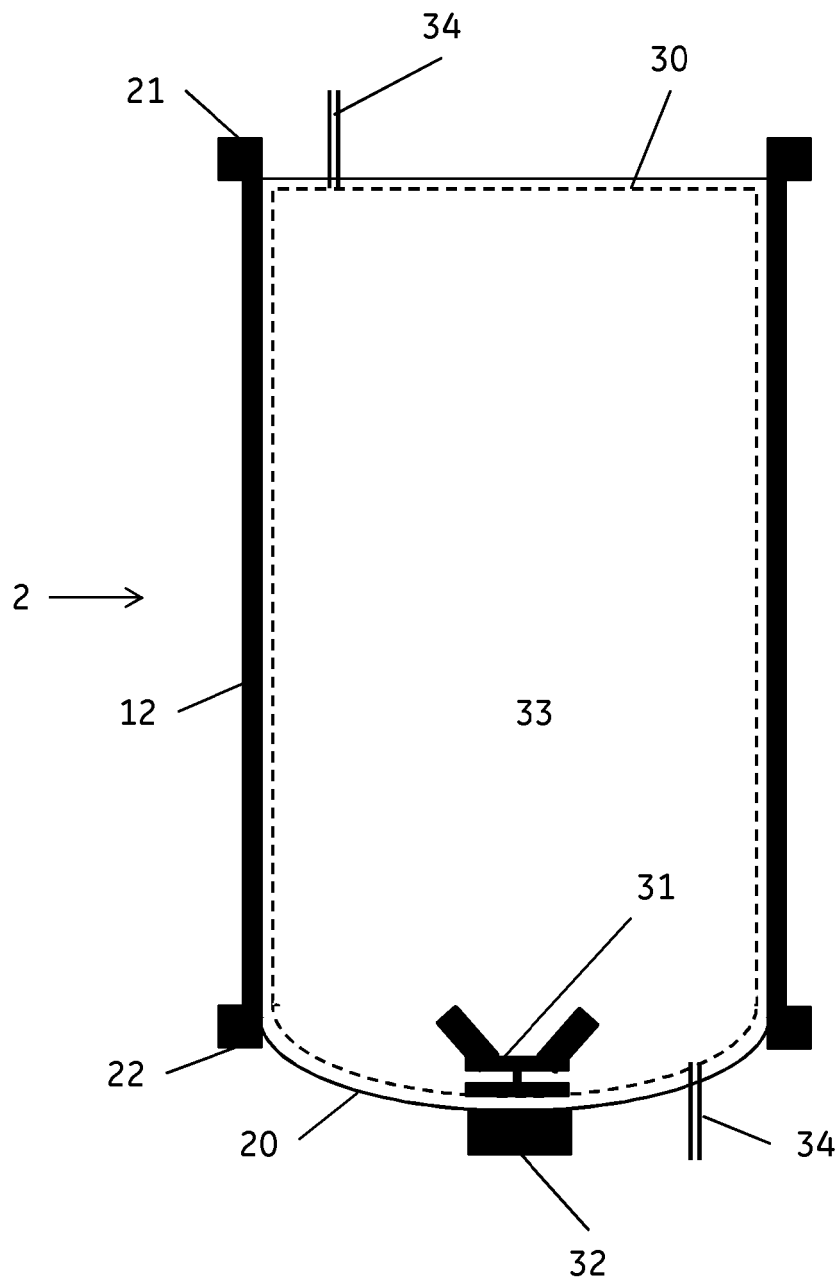


Fig. 9

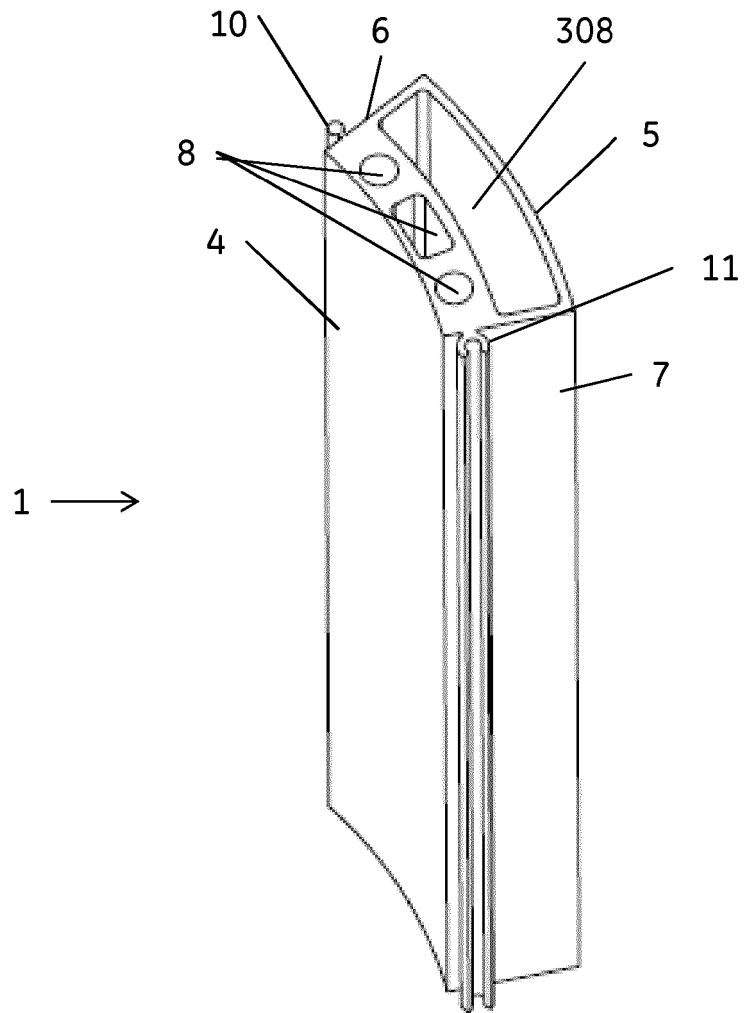


Fig. 10

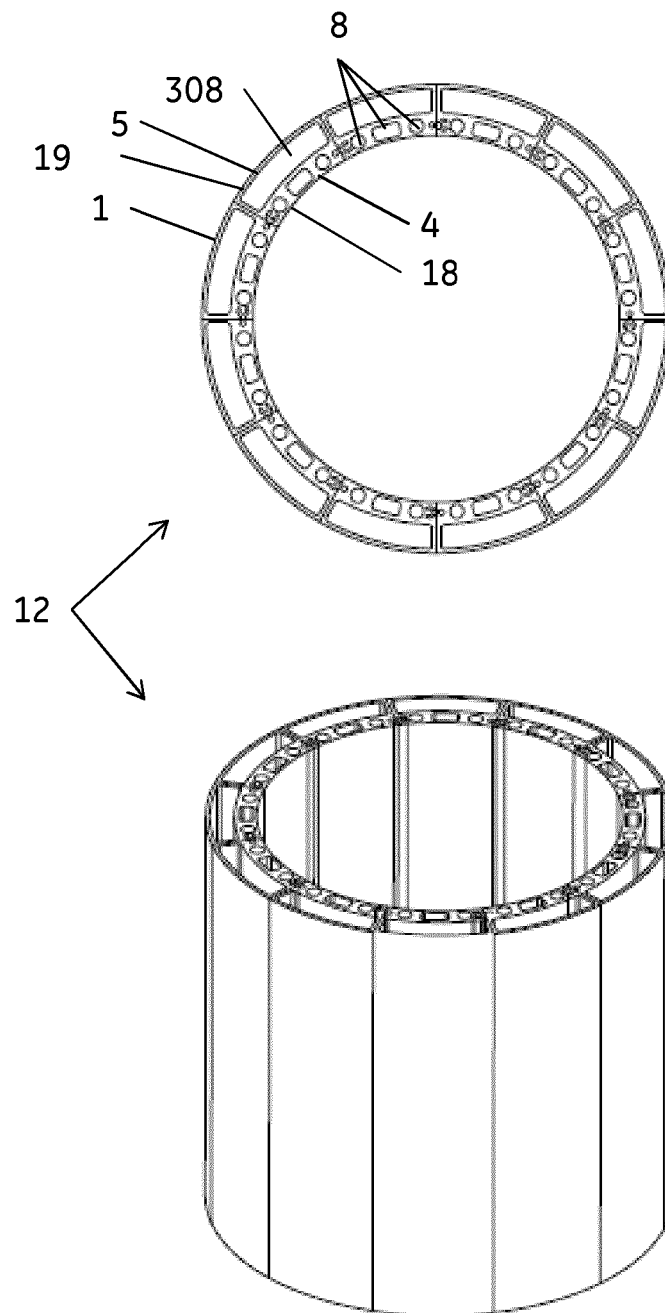


Fig. 11

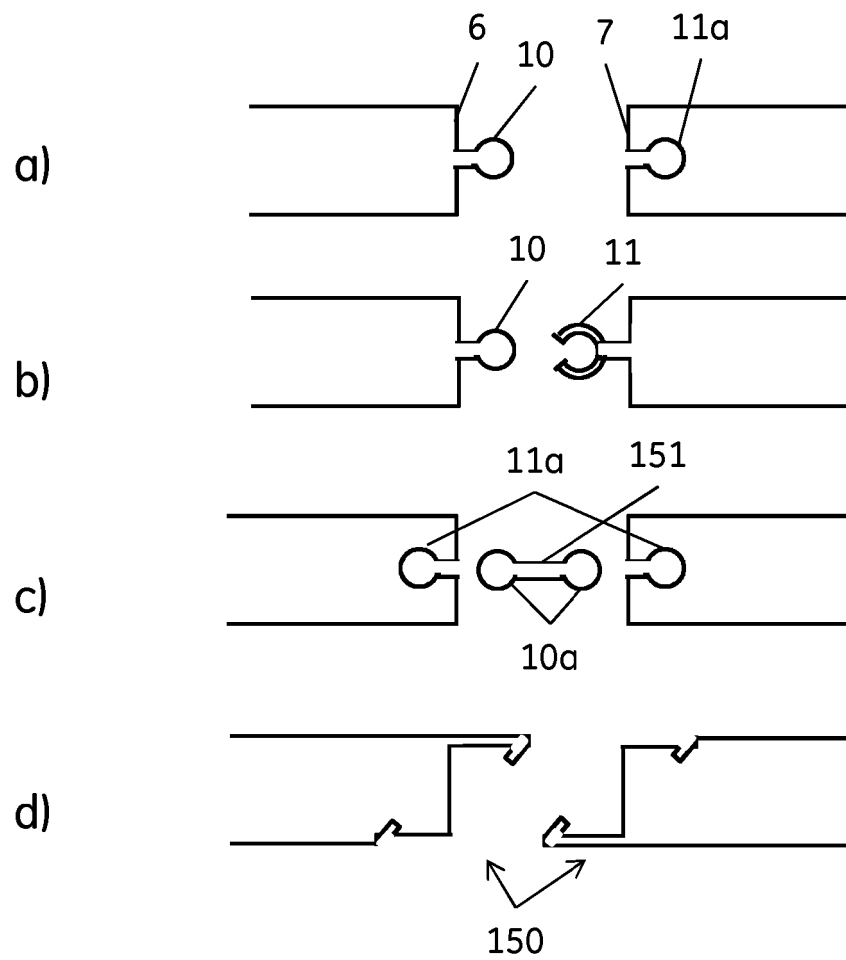


Fig. 12

REFERENCES CITED IN THE DESCRIPTION

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